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March 23, 2001

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on HPV Test Plan and Robust Summaries for C5 Noncyclics Category

Dear Administrator Whitman:

The following comments on the American Chemistry Council's (ACC's) test plan for the C5 noncyclics category are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, The Humane Society of the United States, The Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine million Americans.

The ACC has judiciously formed chemical categories and coordinated with other forthcoming High Production Volume (HPV) test plans. However, the problems that remain with the plan reflect the overall HPV program's flaws and failures. **Blindly conducting the SIDS battery of tests on mixtures of isoprene and 2-methyl-2-butene will contribute nothing to the understanding of these chemicals' toxicities, and indicates a complete disregard for existing data and the current level of knowledge about these and related chemicals.**

Dosing animals with an arbitrary selection of mixtures will provide no progress in understanding the toxicity of these mixtures. These tests, in fact, are a step backwards in scientific progress. The current research on these C5 compounds has far surpassed efforts in hazard identification and is focused on understanding and modeling the kinetics, metabolism, and toxicological mechanisms of these chemicals. The crude SIDS battery will offer nothing to the understanding of these chemicals, and if the EPA supports this research, it will set the state of the science back years.

Our main objections to this test plan are as follows:

1. **The test plan does not maximize the use of existing data.**

   The ACC should employ a more thoughtful approach to understanding the systematic toxicity of the C5 alkane and alkene compounds in this category. Toxicity generally increases in these compounds with increasing molecular weight and increasing number of double bonds. Therefore, a comparison of the toxicity of these chemicals to alkanes and alkenes in other categories, such as the ACC's

Butadiene C4 category, would yield a greater level of understanding of the hazard posed by these substances, without conducting further tests.

Conducting animal tests with mixed streams does not enhance the understanding of the chemicals' potential hazards to human health. The proposal defies good science by ignoring evidence suggesting that the mixed streams would be less reactive than the pure stream of the most bioactive compound.

2. The test protocol does not apply "thoughtful toxicology."

The existing data on the chemicals included in the test plan are sufficient to perform a basic hazard assessment of the industrial streams. Isoprene toxicity is well-understood at both an empirical and biochemical level and is considered a potential carcinogen in humans and other animals. Any additional testing of mixtures with a lower percentage of isoprene will not enhance the already comprehensive understanding of this chemical. 2-methyl-2-butene will behave very similarly to the well-studied butene, a simple asphyxiant. This chemical should also be less toxic than isoprene because it has one less double bond.

3. Extreme species differences will obscure any SIDS test results.

As with 1,3 butadiene, great inter- and intra-species differences in the adverse health effects of isoprene have hindered the understanding of the behavior of this potential carcinogen in humans.

4. Extensive existing human exposure data are not considered.

The primary sources of isoprene in the environment are natural emissions from vegetation. Exposure information on isoprene underscores a flaw in the underlying assumption of the HPV program: High production volume does not necessarily translate into high exposure. A study submitted to the EPA's Ozone Transport Assessment Group (OTAG) Air Quality Analysis Workgroup in 1997, revealed that environmental concentrations were typically orders of magnitude below recommended exposure limits.

5. The ACC test plan does not maximize the use of nonanimal tests.

The ACC is proposing to repeat *in vivo* genetic toxicity tests, even though the toxicity of isoprene has been established and it is an accepted animal carcinogen. Aquatic toxicity tests are proposed on mixed industrial streams, even though these substances are gases, are unlikely to undergo hydrolysis reactions, and have a low water solubility, resulting in rapid volatilization from water.

These concerns reflect specific violations of the EPA's Federal Register notice "Data Collection and Development on High Production Volume (HPV) Chemicals"[1] and the following key items of the EPA's October 14, 1999, letter to HPV participants,[2] which outlined certain principles to minimize animal tests in the program:

1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach.
2. Participants shall maximize the use of existing and scientifically adequate data.
3. Participants shall maximize the use of existing and scientifically appropriate

categories of related chemicals and structure activity relationships.

5. Participants are encouraged to use *in vitro* genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.
8. …As with all chemicals, before generating new information, participants should further consider whether any additional information would be useful or relevant."

For the HPV program to reduce the amount of repetitive, uninformative animal testing, the EPA must require that the ACC perform a more thoughtful review of existing data, expand the development of structure activity relationships, and specifically explain why any additional animal testing is necessary for these compounds. The current understanding of these chemicals has surpassed the stages of crude hazard identification. No further animal testing on these well-studied chemicals should be conducted under the HPV program.

I can be reached via telephone at 202-686-2210, ext. 302, or via e-mail at <ncardello@pcrm.org>. Correspondence should be sent to my attention at the following address: PCRM, 5100 Wisconsin Ave., Suite 400, Washington, DC 20016. I look forward to your response on this important issue.

Sincerely,

Nicole Cardello, MHS
Research Coordinator

Attachment: Specific Comments

cc: The Honorable Robert C. Smith
The Honorable F. James Sensenbrenner, Jr.
The Honorable Ken Calvert
The Honorable Jerry Costello
Council on Environmental Quality
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